

## THE WILLIAM ALLAN MEMORIAL AWARD

Presented to Frank H. Ruddle, Ph.D., at the annual meeting  
of the American Society of Human Genetics,  
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Introduction by

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The William Allan Memorial Award is this Society's highest, indeed only, prize. It honors each year a distinguished contributor to human genetics, and it also honors the memory of a pioneer medical geneticist. I cannot resist pointing out that Dr. William Allan, Jr., was a native Marylander, having been born near Baltimore in 1881, on the grounds of McDonough School in Owings Mills. Col. William Allan, Sr., was the first headmaster (principal) of the farm school, which philanthropist James McDonough had endowed. The school was established to provide an education and wholesome rural upbringing for "destitute and needy boys" aged 4 to 16 years from the City of Baltimore, the State of Maryland, and other maritime cities, in that order of priority. McDonough School still exists today, and its main building is called Allan Hall, but few of its students (which now include girls) can be considered destitute.

William Allan, Jr., studied medicine in Baltimore and practiced internal medicine in Charlotte, North Carolina, for over 30 years before going into medical genetics full-time. He studied human genetics and hereditary diseases for many years, partly in collaboration with Larry Snyder, then at North Carolina State University in Raleigh. With Snyder, he collected, for example, data that confirmed the single-locus basis of the ABO blood groups. Allan pointed to genetic heterogeneity in disorders such as Charcot-Marie-Tooth disease and retinitis pigmentosa and to the differences in natural history in autosomal dominant, autosomal recessive, and X-linked forms of these disorders.

In the last 4 years of his life, Dr. Allan moved his residence from Charlotte to Winston-Salem, becoming a full-time member of the faculty of the then new Bowman Gray Medical School. He was, perhaps, the first American physician to devote himself full-time to medical genetics, although he may share this dis-

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inction with Madge Macklin. (Tinsley Harrison, whose name is well known for his textbook of medicine, was the first professor of medicine at Bowman-Gray.) As Nash Herndon points out, Dr. William Allan died in the line of duty, having developed pneumonia while doing fieldwork in the mountains of western North Carolina.

This year's Allan Awardee was born in New Jersey of British parents, did most of his growing up in Cincinnati, and after a tour of duty in the Air Force, received his college education at Wayne University in Detroit. While he was a full-time premed student, he was also a full-time laboratory worker at Children's Research Center in Detroit. He was hired for that job by the director, Wolf Zuelzer, formerly an active member of this Society. It was this work experience in the laboratory of virologist Cy Stulberg that got Frank hooked on cultured cells, an addiction he has never kicked. He also was exposed to the techniques of electrophoresis (remember, this was the mid-1950s), which were in use in the laboratory for the study of hemoglobin variants and which were to play an important methodologic role in Frank's subsequent scientific career.

Ruddle decided to abandon his medical career goal and go for a Ph.D. instead. To what extent medical school admissions committees helped Frank in that decision I do not know; at any rate, it was a good decision. He went to Berkeley to work for the Ph.D. under Morgan Harris, studying the chromosomes of cultured mammalian cell lines. Finishing his Ph.D. in 1960, he then went to Glasgow for postdoctoral training with Profs. John Paul and Pontecorvo. Ruddle was attracted by Pontecorvo's somatic recombination system. In Glasgow at that time, the possibility of studying mammalian genetics in cultured cells by surrogate methods (which Pontecorvo termed parasexual) was much the talk.

In 1961, Ruddle became an assistant professor to Yale's Biology Department, of which he was to be the chairman from 1977 until recently, when he went on sabbatical. He moved into the laboratories of the venerated Ross Harrison, who is generally acknowledged as the father of tissue culture (work that he started at Johns Hopkins in the first decade of this century).

Soon after getting to New Haven, Ruddle obtained a grant from the recently formed National Institute of General Medical Sciences under the title "the genetics of somatic cells." The grant still continues—something of a record, I should think. Ruddle looked for cell markers useful in somatic cell genetic studies and demonstrated that isozymes are stably expressed codominant gene markers in cultured mouse cells.

Following the work of Barsky, Ephrussi, and others, the demonstration by Weiss and Green (1967) that genes can be mapped by analysis of interspecies somatic hybrids found a prepared mind in Frank Ruddle. Together with a group of bright and enthusiastic students, he embarked on a cartographic expedition exploring the human genome. No single laboratory has contributed as much to our present knowledge of the human gene map. The mouse map was pursued in parallel with the discovery of a surprising degree of homology of autosomal synteny. Ruddle, as much as any single person, made the 1970s for human genetics the decade of somatic cells, just as the 1980s are likely to be remembered as the decade of molecular methods in human genetics. And the mapping was all done

in the context of regulation of gene expression, the enigmas of differentiation and development, gene transfer into cells, and possibilities of eventual gene therapy.

In the last 22 years, many students, both predoctoral and postdoctoral, have passed through Frank's laboratory. Frank has always been concerned for the welfare of his students, both when they are with him and in their subsequent careers.

Another notable feature of Ruddle's style is "unflappability"—an imperturbability even under most stressful circumstances. If he had gone into medicine, this trait combined with sensitivity would have done credit to the Oslerian ideal of *Aequanimitas*.

Two important parascientific contributions of Ruddle are the Camden Cell Bank and the Human Gene Mapping Workshops. It is my understanding that Ruddle was responsible for the conceptualization of the Cell Bank and was a persuasive advocate for it from its beginnings under the aegis of the NIGMS. The usefulness of cell lines with chromosomal rearrangements for regional gene mapping was prominent in Frank's mind.

The seven Human Gene Mapping Workshops, the first six sponsored exclusively by the March of Dimes, were initiated by Ruddle at Yale in 1973. The conferences bring together the aficionados in the field for collation and scrutiny of the latest mapping data. It is certain that the rapidly accumulating information on the human gene map could not have been collected so comprehensively or so authoritatively without the conferences, and they undoubtedly stimulated additional work in particularly fruitful directions. Without counting antigens newly identified by monoclonal antibodies and other antisera, polypeptides separated by two-dimensional O'Farrell electrophoresis, and anonymous DNA segments that have been mapped, the most recent conference in Los Angeles (under the able organization of Dr. Robert Sparkes and his group) brought the total to slightly over 600 gene loci, for which the chromosomal location and, in some instances, regional location are known.

I have taken many photographs of Frank, at Bar Harbor where he has been a frequent lecturer in the Short Course in Medical Genetics, at HGM workshops, and on other occasions, many of them with his wife Nancy, an immunologist and able scientist in her own right, as well as pictures with his daughters, but I shall not show you any of these because we have the real thing with us this evening. Frank is himself a hybrid of Cornish and Welsh ancestry. His Welsh ancestry is reflected in his bushy eyebrows, which, when less well trimmed than now, resemble those of fellow Welshman, union boss John L. Lewis, and his physique and stature are Lincolnesque, and I do not mean Marfanoid.

It is a great personal pleasure to introduce to the members of the American Society of Human Genetics the 1983 Allan Awardee: Dr. Frank Ruddle.